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Molecular Recognition: Hydrogen bonding induced configurational locking of a new Photoresponsive receptor by Dicarboxylic acids

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Abstract: A new photoresponsive system **1** has been synthesised and recognition by the cavity of the *cis*-isomer of **1** of dicarboxylic acids of various chain lengths has been studied on irradiation at 310 nm. The cavity of the *cis* form is found to be selective for adipic acid.

Key words: Molecular recognition, photoresponsive receptor.

Photoresponsive systems are currently attracting much attention because of their many possible applications in diverse fields of science and technology [1-4]. Azo compounds and their derivatives provide such photoresponsive systems which undergo conversion from the *trans*-to *cis*-forms on irradiation with UV light (λ = 310 nm) in solution (although the ground state is mostly populated with the *trans*-form and reverts to the original *trans*-form on thermal isomerisation). This photochemical switching leads to two photostationary equilibria based on *cis-trans* populations [5-8].

Shinkai *et al.* reported a crown ether containing an aza-photoresponsive receptor [9] which was found to promote photocontrolled extraction and transport of ions across artificial membranes. Photocontrolled reversible association- dissociation phenomena with an ammonio-alkyl lariat in a crown-ring containing an aza- photofunctional system was also studied by Shinkai *et al* [10]. Azobenzenes have also covalently incorporated into the backbone and also in the chain of many polymers to study the kinetics of *cis-trans* photoisomerisation of benzene residues in relation to the molecular weight and flexibility of the polymer chain [11-12].

Thus, based on such photochromic behaviour of azobenzenes, we report here a functionalised azo compound **1** having carboxyl binding units at both ends and capable of showing *cis-trans* isomerisation on photoirradiation (though the ground state is mostly *trans*). The cavity of the *cis-isomer* of the photoresponsive system **1** obtained on UV irradiation, selectively recognises adipic acid.

Receptor **1** [13] was synthesised (scheme 1) from azobenzene dicarboxylic acid [8] **2** by coupling

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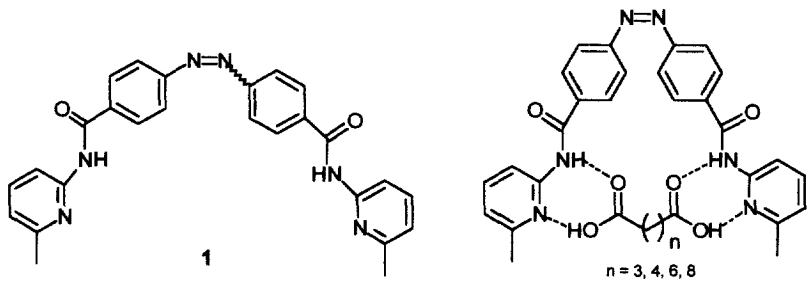
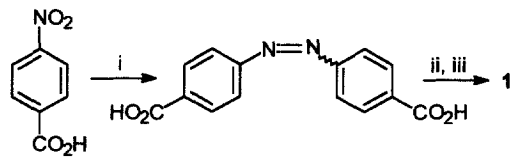


with 2- amino-6-methylpyridine. Compound **1** was isolated in 75% yield.



Scheme 1: i) Glucose, NaOH, ii) PCl_5, 1,2-dichlorobenzene, iii) 2-amino-6-methylpyridine, CH_2Cl_2.

Complexation studies were carried out by NMR titrations as well as by UV experiments using a series of dicarboxylic acids of different chain lengths. As the ground state of the receptor **1** is mostly populated with the *trans*-form, NMR titration experiments (in $CDCl_3$ solutions containing 2% d_6-DMSO) give an idea about the complexation ability of the *trans*-form. The weak binding of dicarboxylic acids with the *trans*-form of **1** (K_a for glutaric is < 150 M^{-1}; adipic: 1.50 x 10^2 M^{-1}; suberic: 5.32 x 10^2 M^{-1} and sebacic : 1.76 x 10^2 M^{-1}) is due to the lack of formation of tight complexes with the *trans*-geometry. In case of glutaric and adipic acids, binding with the *trans*-form of **1** is significantly weaker and sigmoidal NMR titration curves are observed indicating that other competing modes of binding occur. For long chain suberic and sebacic acids with the *trans*-form, the break in the titration curves ($\Delta\delta$ vs C_{guest}/ C_{host}) at 0.5 and 1.0 establishes a 2:1 and 1:1 (host : guest) stoichiometry [14] respectively. Our prime objective is to see the interaction of dicarboxylic acids of various chain lengths with the *cis*-form of **1**. Accordingly, UV experiments were performed to study the chain length selectivity by the cavity of the *cis*-isomer of receptor **1**. The *cis*-isomer of **1** on irradiation at 310 nm, is locked in the presence of aliphatic dicarboxylic acids by the formation of hydrogen bonds, as predicted in complex **2**. Formation of this 1:1 complex brings an additional stabilisation of the *cis*-configuration over the *trans*-form of **1** and the extent of stabilisation is strongly dependent on the formation of a tight complex **2** which, in turn, is attributed to the matching of the chain length of dicarboxylic acid with the cavity size of the *cis*- form of receptor **1**.

The positioning of the pyridine amides for binding to the dicarboxylic acids by a suitable spacer is important as shown by the terephthaloyl spacer for adipic acid [15] and the Troger's base spacer for

suberic acid [16]. Here the cavity of the *cis*-form of the receptor **1**, where two pyridine amide binding motifs are flanked by a photochemical switching azo unit, is found to be specific for adipic acid.

The absorption spectrum of compound **1** in acetonitrile (c 4.44 x 10^{-5} M) shows a strong band at 335 nm and another centered at 286 nm. On irradiation of the compound with 310 nm light, obtained from a high pressure xenon lamp coupled with a monochromator, the energetically preferred ground state *trans*-form goes to the *cis*-form via a photochemical isomerisation process. The experiments were performed with the receptor **1** in the presence or absence of dicarboxylic acids and the absorption spectrum of **1** was recorded at different time intervals under irradiation. The absorbances at λ_{max} = 335 nm were plotted against time and were found to be fairly linear before the photostationary state is reached.

The *cis*-form is deduced from the decrease in absorbance (OD) with irradiation time (Fig. 1) (assuming initially the compound is 100% trans) and maximum decrease in OD with time with adipic acid (Fig.2) suggests the tight fitting of the chain into the cavity so that the second step of the following equilibria is shifted more towards the forward direction leading to fast *cis-trans* isomerisation.

$$Trans \underset{}{\overset{h\nu}{\rightleftharpoons}} Cis \overset{\text{dibasic acid}}{\rightleftharpoons} Cis\text{-(Hydrogen bonded)}$$

Binding studies† [17] in CH_3CN at 25^{0}C using UV-VIS spectroscopy show that adipic acid binds to the *trans* form **1** with a binding constant of 5.16 x 10^3 M^{-1}. Here also the sigmoidal titration curve indicates the several modes of competing binding of the *trans* isomer with adipic acid. In comparison, on irradiation at 310 nm in CH_3CN, the *cis*-form of **1** binds adipic acid with 1:1 stoichiometry by a K_a value of 1.81 x 10^4 M^{-1}.

In this context, the fully extended conformation of the dicarboxylic acids is more prevalent than the coiled conformation. Dicarboxylic acids with shorter chain lengths that are unable to bridge the two pyridine rings, cannot form the 1:1 complex **2**, necessary to lock the *cis*-isomer of the receptor **1** and this situation is analogous to a free receptor leading to a fast *cis-trans* isomerisation. Similarly, if the 1:1 complex (as suggested in complex **2**) is loose enough, the *cis*-form, having little stabilisation, will go to the *trans*-form quickly. If the chain length is larger than the cavity dimension there is also no possibility of formation of 1:1 complex **2**. In this regard, formation of 1:1 complexes leading to a dynamic supramolecular structure in solution (i.e. receptor and substrate alternately interlinked) cannot be ruled out. But this situation is also similar to the uncomplexed state having a stabilisation of the *trans*-form over the *cis*-form.

The rate of isomerisation of the receptor **1** in the presence of glutaric acid or long chain sebacic acid is almost similar in magnitude but is distinctly modified in the presence of adipic acid. This suggests the formation of a tighter 1:1 complex with adipic rather than glutaric and sebacic acids.

We have thus shown for the first time that the cavity dimension of the *cis*-isomer of the new azo photoresponsive receptor **1** is selective for adipic acid. Further studies in our laboratory are in progress

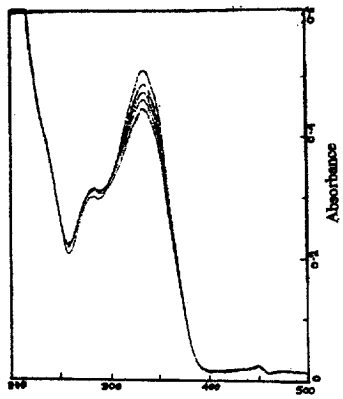


Fig. 1

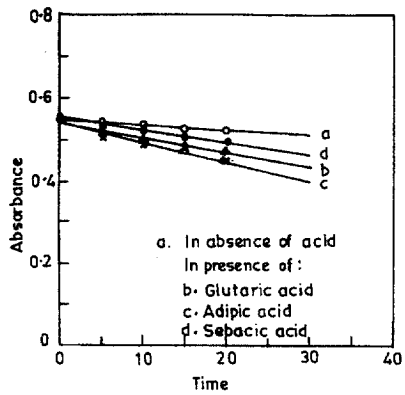


Fig. 2

to explore this idea in transport phenomena.

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† UV titrations (CH_3CN): In determining a K_a value with the *trans* form of **1**, a solution of the *trans*- form of **1** (8.8 x 10^{-5} M) in CH_3CN was used and the absorption was followed at different wavelengths on successive addition of guest solution. The binding constant was determined by Benesi - Hildebrand plot (given in ref. 17). Similarly, in determining a K_a value with the *cis*-form of **1**, different sets of stock solutions of *trans*-form with adipic acid of varying composition were prepared. After passing UV light (310 nm) absorption at 335 nm was recorded for each set and the binding constant was determined by the same method.

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[13] **Compound 1** (mp. 268-270°C), M^+ 450.3 (25.63%), ^1H NMR (200 MHz, $CDCl_3$) δ: 8.65 (s, 2H, NH), 8.21 (d, 2H, J = 8Hz), 8.12 (d, 4H, J = 8 Hz), 8.06 (d, 4H, J = 8 Hz), 7.68 (t, 2H, J = 8 Hz), 6.97 (d, 2H, J = 8 Hz), 2.50 (s, 6H). ^{13}C-NMR (50 MHz, $CDCl_3$): 164.62, 156.87, 154.36, 150.56, 138.80, 136.53, 128.25, 123.30, 119.58, 111.00, 23.85.
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